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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,077	04/23/2007	Diana Helen Pliura	RAM-PT015	8083

3624 7590 10/28/2010  
VOLPE AND KOENIG, P.C.  
UNITED PLAZA  
30 SOUTH 17TH STREET  
PHILADELPHIA, PA 19103

EXAMINER
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HIRIYANNA, KELAGINAMANE T

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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10/28/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

eooffice@volpe-koenig.com  
hrivera@volpe-koenig.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/580,077	<b>Applicant(s)</b> PLIURA ET AL.	
	<b>Examiner</b> KELAGINAMANE HIRIYANNA	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 27 July 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-78 and 117-121 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-78 and 117-121 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Election/Restrictions*

Applicant's response filed on 07/27/2010 in response to office action mailed on 02/01/2010 has been acknowledged.

Claims 1-9, 12-13, 17-19, 22-23, 25-30, 32-33, 37-49, 52-53, 57-59, 62-63, 65-66, 69-78 and 117-119 are amended.

Claim 31 is canceled.

*Applicant's amendments to claims after previous Election/Restriction and the scope and nature of the amended subject matter are such that, the claims require a further restriction.*

### **37 CFR 1.142(a) provides that restriction is proper at any stage of prosecution up**

*to final action, a second requirement may be made when it becomes proper, even though there was a prior requirement with which applicant complied. Ex parte Benke, 1904C.D. 63, 108 O.G. 1588 (Comm'r Pat. 1904).*

*The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300**.*

Claims 1-30, 32-78 and 117-120 are under Election/Restriction.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1A. Claim(s) 1, 3-9, 13, 14-30, 32 and 118, 120 drawn to a autoclaved liposome composition wherein pH of the aqueous medium within liposome is less than the pKa of the lipophilic amine.

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Group1B. Claims 1 & 2 , drawn to a liposome composition wherein pH of the aqueous medium within liposome is equal to pKa of the lipophilic amine.

Group 1C. Claims 1&10 drawn to a liposome that further comprises cholesterol.

Group 1D. Claims 1, 11-12 drawn to a liposome that further comprises ethanol.

Group1E. Claims 1 & 33-40 drawn to a liposome composition that is physically or chemically stable over one year

Applicant further should note that the above inventions group (Group IE) is tentatively placed with base claim 1. Claims 33-40 are currently claimed as dependent from a canceled claim 31. Applicant should correct the same for any further consideration of this invention.

Group F. Claims 41-49, 53-65 & 119 drawn to a sterile and stable liposome composition wherein the pH of the aqueous medium within liposome is less than or equal to pKa of the lipophilic amine.

Group 1G. Claims 41 and 50 drawn to sterile and stable liposome composition further comprising cholesterol.

Group 1H. Claims 41, 51-51 & 66-78 drawn to a sterile and stable liposome composition further comprising ethanol.

Group1I. Claims 41 and 117 drawn to a sterile and stable liposome composition undergoing changes in specific multiple components.

1. The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The instant claims share a common technical feature, namely stable and/or sterile liposomes, wherein said liposomes comprise a suitable aqueous medium, a suitable phospholipid and at least one pharmaceutical agent comprising a lipophilic amine and a pharmaceutically acceptable acid or an organic salt of a lipophilic amine and an optional organic acid. However, this common technical feature is not considered a special technical feature since it does not make a contribution over the prior art. For example, Steel et al. (US Patent No. 6224853) discloses aqueous compositions comprising liposomes, wherein the liposomal material may include phospholipids. In one particular embodiment, Steel et al. teach the incorporation of fentanyl citrate (an organic acid of a lipophilic amine), see Table 3, into the liposomal compositions of the invention. Moreover, in regards to the sterilization of liposomes, this process is also known in the art, see for example Kikuchi et al. (1991, Chem. Pharm. Bull., 39(4), pp. 1018-1022) teach a method for the

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sterilization of liposomes, therefore this aspect of the claimed invention is also well known in the prior art. Still further Mezei et al (US Patent No. RE38,407E) disclose a stable and sterile liposome composition described by instant invention; Camu et al (US Patent No. 6,149,937) also disclose a stable sterile composition of liposomes of instant invention. Thus, the technical features in common with the recited invention groups are not considered special technical features; therefore the invention groups are determined to lack unity of invention.

2. Additionally, as per 37 CFR 1.475(b)-(c), since the instant application contains claims directed to more than one category of invention, the instant invention groups are not considered to possess unity of invention, see below:

§ 1.475 Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage.

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.

3. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

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requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

4. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Pharmaceutical agents selected from:

(i) a lipophilic amine and a pharmaceutically acceptable acid, wherein the pharmaceutically acceptable acid is selected from an organic or inorganic acid, and

(ii) a pharmaceutically acceptable organic acid salt of a lipophilic amine, and optionally a pharmaceutically acceptable acid comprising a pharmaceutically acceptable organic acid.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

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Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. The claims are deemed to correspond to the species listed above in the following manner:

The following claim(s) are generic: Claims 1-129 are generic with respect to the recited species.

6. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The recited species are considered to lack unity of invention for the same reasons set forth above as they relate to the unity of invention of the invention groups recited above

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanne Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633